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Do high $PaCO_2$ levels during discharge from the hospital predict medium-term mortality in chronic respiratory failure patients without domiciliary non-invasive mechanical ventilator?

Hastaneden taburculuk sırasında yüksek $PaCO_2$ seviyeleri, evde non-invaziv mekanik ventilatörü olmayan kronik solunum yetmezliği hastalarında orta vadeli mortaliteyi öngörüyor mu?

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ABSTRACT

Aim: Long-term domiciliary use of a non-invasive mechanical ventilator (NIV) is a controversial form of therapy for patients with chronic obstructive pulmonary disease (COPD) and moderate hypercapnia. The present research attempted to examine hospital admissions, hospitalizations, and medium-term (6-8 months) mortality in a group of patients with compensated but moderate hypercapnia who were discharged from our clinic without a domiciliary NIV.

Material and Method: The sample of this retrospective, observation-based cohort study consisted of compensated hypercapnic cases that were hospitalized in our Pulmonology Intensive Care Unit (ICU) between 01.01.2019 and 12.31.2020.

Results: A total of 245 patients discharged with high partial pressure of carbon dioxide ($PaCO_2$) levels between 01.01.2019 and 12.31.2020 were included in the study. While 58% of the cases were males (n=142), we found the mean age of the patients to be 71.89±12.63 years. The findings yielded no significant differences between the groups by sex, use of NIV during hospitalization, number of days of NIV use during hospitalization, use of LTOT or Oxygen tube at home, and intubation history before ICU admission ($p>0.05$). Similarly, we could not conclude significant differences between the groups by hospitalization, discharge, and follow-up arterial blood gas (ABG) parameters. Yet, the rates of congestive heart failure, coronary artery disease, and atrial fibrillation were significantly higher in the mortality group ($p=0.017$, $p=0.032$, and $p=0.002$, respectively). Besides, high $PaCO_2$ levels versus mortality rates at 1, 3, 6, 8, and 12 months and in the entire follow-up period were subjected to the ROC analysis. Accordingly, when accepting 50.25 mmHg as the cut-off value for determining the 8-month mortality for discharge $PaCO_2$ levels, we calculated the sensitivity to be 78.6% and the specificity to be 43%.

Conclusion: Overall, it is highly convenient to consider the possible positive effects of NIV therapy on mortality among patients with heart-related diseases and with moderate hypercapnia ($PaCO_2$>50 mmHg) at discharge.

Keywords: Respiratory failure, hypercapnia, mortality, ventilation

ÖZ

Amaç: Uzun süreli evde NIV kullanımı, kompanse ılımlı hiperkapnik KOAH olan hastalar için tartışmalı bir tedavi şeklidir. Çalışmamızın amacı kliniğimizden taburcu edilen kompanse fakat ılımlı hiperkapnik hastalardan evde non-invaziv mekanik ventilatörü olmayan hasta grubunun taburculuk sonrası hastaneye başvuru sayıları, hastaneye yatış sayıları ve orta vadeli (6-8 ay) mortalite durumlarını incelemektir.

Gereç ve Yöntem: Çalışma grubunu oluşturan hastalar 01.01.2019 ve 31.12.2020 tarihleri arasında Göğüs Hastalıkları Yoğun Bakım Kliniğinde yatarak tetkik edilip taburcu edilmiş kompanse hiperkapnik olgulardan oluşmaktadır. Araştırmamız retrospektif gözleme dayalı kohort çalışma olarak planlanmıştır.

Bulgular: Çalışmaya 01.01.2019 ve 31.12.2020 tarihleri arasında yüksek $PaCO_2$ düzeyiyle taburcu edilmiş toplam 245 hasta dahil edildi. Olguların %58'i erkek (n=142) cinsiyette idi. Hastaların yaş ortalaması 71,89±12,63 idi. Her iki grup arasında cinsiyet, yatışları sırasında NIV kullanımı, yatışları sırasında NIV kullanım gün sayısı, evde USOT veya Oksijen tüpü kullanımı ve GYBÜ yatışı öncesinde entübasyon öyküsü bulunması açılarından istatistiksel olarak anlamlı farklılık bulunmamaktadır ($p>0,05$). Mortalite grubunda konjestif kalp yetmezliği, koroner arter hastalığı ve atriyal fibrilasyon bulunma oranları istatistiksel olarak anlamlı düzeyde daha yüksektir (sırasıyla $p=0,017$, $p=0,032$ ve $p=0,002$). Her iki grup arasında yatış, taburcu ve kontrol sonuçları açısından istatistiksel olarak anlamlı farklı izlenmemiştir. Yüksek $PaCO_2$ düzeyiyle taburcu olmuş olguların 1, 3, 6, 8, 12 aylık ve takip süresinin tamamındaki mortalite oranlarına karşılık taburculuk $PaCO_2$ düzeyleri ROC analizine tabi tutulmuştur. ROC analizi sonucunda, taburculuk $PaCO_2$ düzeyleri için 8. ay mortaliteyi belirlemede cut-off değeri 50,25 mmHg sınır değer kabul edildiğinde, duyarlılık %78,6 özgüllük %43 olarak hesaplanmıştır.

Sonuç: Taburculukta ılımlı hiperkapnisi ($PaCO_2$>50 mmHg) olan, kalp ilişkili hastalığı bulunan hasta grubunda evde NIV tedavisinin dikkatle değerlendirilmesi gerektiğini düşünüyoruz.

Anahtar Kelimeler: Solunum yetmezliği, hiperkapni, mortalite, ventilasyon

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INTRODUCTION

Respiratory failure is a syndrome resulting from inadequate oxygenation of mixed venous blood and/or carbon dioxide elimination and is often considered under two categories. On the one hand, hypoxemic respiratory failure is described as the arterial partial pressure of oxygen (PaO_2) less than 60 mmHg while breathing room air at rest. Hypercapnic respiratory failure, on the other hand, develops as a result of ventilation failure and is characterized by an increase in arterial partial pressure of carbon dioxide ($PaCO_2$) above 45 mmHg (1). The only physiopathological mechanism that specifies the $PaCO_2$ level is alveolar ventilation.

Diseases reducing minute ventilation or increasing dead space ventilation result in hypercapnia. Although the increase in $PaCO_2$ can be compensated by increasing alveolar ventilation, increased ventilation requirements cannot be met, which, in turn, may lead to hypercapnia with any underlying lung disease, respiratory muscle fatigue, or decreased $PaCO_2$ sensitivity of the respiratory center (2). Since its invention, non-invasive mechanical ventilation (NIV) has been growingly used for the treatment of patients with chronic obstructive pulmonary disease (COPD) and chronic stable hypercapnia. It is particularly utilized in respiratory failure developing during acute exacerbations of COPD because previous research consistently showed its positive impact on survival (3). However, few studies have addressed the domiciliary use of NIV for patients with stable hypercapnic COPD so far. Even most of these limited studies employed small numbers of patients and/or used a low pressure to normalize gas exchange, improve symptoms, and reduce morbidity and mortality (4).

Some studies concluded that long-term use of NIV improves physiological parameters (e.g., lung function or gas exchange), clinical symptoms (e.g., functional capacity, dyspnea, quality of life, and sleep quality), and patient-centered outcomes (e.g., hospital readmission and mortality rates) in stable patients with chronic hypercapnia (resting $PaCO_2$>45 mmHg and above; COPD in stable period) (5,6). On the other hand, there is still insufficient evidence that long-term NIV treatment increases life expectancy and reduces mortality (7). The long-term use of NIV is a controversial form of therapy for patients with moderate hypercapnic COPD. While there is no doubt that chronic nocturnal NIV administration improves outcomes in patients with restrictive lung diseases and neuromuscular diseases (8), there is conflicting evidence of its long-term benefits in COPD patients (9,10); thus, long-term NIV practice for COPD varies significantly across Europe (11).

Respiratory failure cases presenting with acute or chronic exacerbation are frequently hospitalized in the Pulmonary Intensive Care Unit (ICU) of tertiary hospitals for chest diseases (level II intensive care service is provided). Besides, COPD is blamed for respiratory failure in most patients.

Our study attempted to evaluate arterial blood gas (ABG) parameters of the patients, admissions to the hospital or emergency department, hospitalizations, and medium-term (6-8 months) mortality in a group of compensated but moderate hypercapnic patients who were discharged from our clinic without domiciliary NIV.

MATERIALS AND METHOD

Health Sciences University, Keçiören Training and Research Hospital, Clinical Research Ethics Committee granted ethical approval to our study (Date: 11.09.2021, Decision No: 2012-KAEK-15/2405). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The sample of this retrospective, observation-based cohort study consisted of compensated hypercapnic cases that were hospitalized in our Pulmonology ICU (PICU) between 01.01.2019 and 12.31.2020.

Patient Selection

The inclusion criteria included receiving inpatient treatment in a PICU, having available follow-up data, having a $PaCO_2$ value above 45 mmHg in ABG taken just before discharge, and not possessing a domiciliary NIV. Nevertheless, patients without available data, those with a $PaCO_2$ value of 45 mmHg and below in ABG before discharge, and patients who had a domiciliary NIV or had been prescribed an NIV at discharge were not included in the study.

We investigated readmissions to the emergency department after discharge with high carbon dioxide levels, intensive care admissions, numbers of outpatient visits, and mortality rates. The data included all admissions, hospitalizations, and mortality cases until 30.06.2021. In this respect, we extracted and analyzed a maximum of 19 months of follow-up data of the first discharged patient and a minimum 7-month follow-up data of the last discharged patient. We then statistically compared the data between the cases with mortality during the follow-up period constituted (mortality group) and others (survivor group).

Statistical Analysis

We analyzed the data using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). The normality of data distribution was checked using the Kolmogorov

Smirnov test, while Levene's test was resorted to evaluate the homogeneity of variances in the data. We showed continuous data as mean±standard deviation and categorical data as number and percentage (n, %) unless stated otherwise. We then compared the groups using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Categorical variables were compared using the Pearson chi-square test or the Fisher exact test. Receiver operating characteristic curve (ROC) analysis was used to determine the threshold value of $PaCO_2$ associated with mortality risk. A p-value<0.05 was considered significant in all statistical analyses.

RESULTS

Of the 245 patients, discharged with high $PaCO_2$ levels, 58% were males (n=142), and 42% were females (n=103). The mean age of the patients was found to be 71.89±12.63 years. The findings revealed that the mortality group was significantly older than the survivors (p<0.001). Moreover, the mortality rates among those treated in a tertiary anesthesia intensive care unit (AICU) before being admitted to the PICU were found to be significantly higher (p=0.037). Yet, we could not reach significant differences between the groups by sex, NIV use during hospitalization, number of days of NIV use during hospitalization, long-term oxygen therapy at home (LTOT), and intubation history before PICU admission (p>0.05). The comparisons of the groups' demographic and other characteristics are given in **Table 1** and **Table 2**.

Table 1. Comparison of demographic and other characteristics between groups

	Mortality group (n=88)		Survivor group (n=157)		Total (n=245)		p
	n	%	n	%	n	%	
Sex (male)	51	58	91	58	142	58	0.999 β
Admission unit (to PICU)							0.037 β
Emergency department	30	34.1	76	48.4	106	43.3	
Ward	1	1.1	5	3.2	6	2.4	
AICU	57	64.8	76	48.4	133	54.3	
NIV use at PICU							0.478 β
No	26	29.5	53	34	79	32.4	
Yes	62	70.5	103	66	165	67.6	
LTOT at home							0.981 β
No	10	11.4	18	11.5	28	11.4	
Yes	78	88.6	139	88.5	217	88.6	
History of intubation							0.796 β
No	81	92	143	91.1	224	91.4	
Yes	7	8	14	8.9	21	8.6	

Categorical variables were expressed as frequency (percentage). Chi-square test β was performed, and p<0.05 was considered significant. PICU: Pulmonary intensive care unit, NIV: Non-invasive mechanical ventilation AICU: Anesthesia intensive care unit, LTOT: Long-term oxygen therapy

Table 2. Comparison of age and number of days of NIV use between groups

	Mortality group (n=88)		Survivor group (n=157)		Total (n=245)		p
	M	SD	M	SD	M	SD	
Age	76.61	10.70	69.24	12.89	71.89	12.63	<0.001*
Number of days of NIV use	4.77	3.68	4.58	3.37	4.65	3.48	0.733*

Continuous variables were expressed as mean (M)±standard deviation (SD). Independent samples t-test * was performed, and p<0.05 was considered significant. NIV: Non-invasive mechanical ventilation

Both groups were also compared by the presence of comorbidity, and the findings yielded that history of cardiac disease (congestive heart failure, coronary artery disease, and atrial fibrillation) was significantly higher in the mortality group (p=0.017, p=0.032, and p=0.002, respectively). Yet, the groups did not significantly differ by the presence of COPD, diabetes mellitus, hypertension, pulmonary thromboembolism, pneumonia, bronchiectasis, chronic kidney disease, lung cancer, interstitial lung disease, kyphoscoliosis, and obstructive sleep apnea syndrome (p>0.05) (**Table 3**).

Table 4 compares the ways of readmission and the rates of readmission in the first 30, 90, 180, and 360 days of discharge between the groups. Accordingly, we found that there were significantly more survivor patients readmitted through the mentioned channels (the emergency department, clinics, wards, and intensive care unit) than the patients with mortality (p<0.05). Similarly, the survivor group had significantly higher readmission rates in the first 90, 180, and 360 days of discharge (p<0.05). Yet, the groups did not significantly differ by readmission rate in the first 30 days of discharge (p=0.162).

The hospitalization, discharge, and follow-up ABG parameters between the groups are shown in **Table 5**. Our results did not yield significant differences between the mentioned ABG test results.

Discharge $PaCO_2$ levels versus mortality rates at 1, 3, 6, 8, and 12 months and in the entire follow-up period were subjected to ROC analysis. The results yielded an area under the procedure characteristic curve (AUC) to be 0.594 for determining the 8-month mortality for the discharge $PaCO_2$ levels, and it was statistically significant (p=0.034). To be able to define a cut-off value for this test, we examined sensitivity and specificity values and focused on the optimum points. Accordingly, when accepting 50.25 mmHg as the cut-off value for determining the 8-month mortality for discharge $PaCO_2$ levels, we calculated the sensitivity to be 78.6% and the specificity to be 43% (**Table 6**).

Table 3. Comparison of comorbidities between the groups

	Mortality group (n=88)		Survivor group (n=157)		Total (n=245)		p
	n	(%)	n	(%)	n	(%)	
Chronic obstructive pulmonary disease							0.957
No	11	12.5	20	12.7	31	12.7	
Yes	77	87.5	137	87.3	214	87.3	
Diabetes mellitus							0.620
No	67	76.1	115	73.2	182	74.3	
Yes	21	23.9	42	26.8	63	25.7	
Hypertension							0.136
No	35	39.8	78	49.7	113	46.1	
Yes	53	60.2	79	50.3	132	53.9	
Congestive heart failure							0.017
No	52	59.1	116	73.9	168	68.6	
Yes	36	40.9	41	26.1	77	31.4	
Coronary artery disease							0.032
No	66	75.0	135	86.0	201	82.0	
Yes	22	25.0	22	14.0	44	18.0	
Atrial fibrillation							0.002
No	77	87.5	153	97.5	230	93.9	
Yes	11	12.5	4	2.5	15	6.1	
Pulmonary thromboembolism							0.999
No	85	96.6	151	96.2	236	96.3	
Yes	3	3.4	6	3.8	9	3.7	
Pneumonia							0.499
No	81	92.0	148	94.3	229	93.5	
Yes	7	8.0	9	5.7	16	6.5	
Bronchiectasis							0.424
No	87	98.9	152	96.8	239	97.6	
Yes	1	1.1	5	3.2	6	2.4	
Chronic kidney disease							0.192
No	84	95.5	155	98.7	239	97.6	
Yes	4	4.5	2	1.3	6	2.4	
Lung cancer							0.657
No	87	98.9	153	97.5	240	98.0	
Yes	1	1.1	4	2.5	5	2.0	
Interstitial lung diseases							0.359
No	87	98.9	157	100.0	244	99.6	
Yes	1	1.1	-		1	0,4	
Kyphoscoliosis							0.999
No	87	98.9	154	98.1	241	98.4	
Yes	1	1.1	3	1.9	4	1.6	
Obstructive sleep apnea syndrome							0.265
No	87	98.9	150	95.5	237	96.7	
Yes	1	1.1	7	4.5	8	3.3	

*Chi-square test. p<0.05

Table 4. Readmissions to the hospital after discharge

	Mortality group (n=88)		Survivor group (n=157)		Total (n=245)		p
	n	(%)	n	(%)	n	(%)	
No readmission	38	48.1	39	25.2	77	32.9	0.004
Emergency department	19	24.1	44	28.4	63	26.9	
General ward	0	-	2	1.3	2	0.9	
Intensive care unit	0	-	1	0.6	1	0.4	
Outpatient clinic	22	27.8	69	44.5	91	38.9	
Readmission in the first 30 days	29	33	66	42	95	38.8	0.162
Readmission in the first 90 days	35	39.8	92	58.6	127	51.8	0.005
Readmission in the first 180 days	40	45.5	104	66.2	144	58.8	0.002
Readmission in the first 360 days	41	46.6	117	74.5	158	64.5	<0.001

*Chi-square test; p<0.05

Table 5. Hospitalization, discharge, and follow-up ABG values between the groups

ABG parameters	Mortality group (n=88)		Survivor group (n=157)		p
	M	SD	M	SD	
Hospitalization pH	7.37	0.08	7.39	0.08	0.226β
Discharge pH	7.46	0.08	7.46	0.05	0.196 β
Follow-up pH	7.42	0.07	7.42	0.06	0.870*
Hospitalization PaO_2	66.78	29.89	62.81	25.48	0.577 β
Discharge PaO_2	58.47	17.37	59.76	19.40	0.658 β
Follow-up PaO_2	64.66	31.38	58.73	21.98	0.430 β
Hospitalization $PaCO_2$	59.90	12.64	60.66	11.63	0.635*
Discharge $PaCO_2$	52.83	5.29	51.57	6.72	0.222 β
Follow-up $PaCO_2$	49.07	10.21	50.83	11.79	0.891 β
Hospitalization HCO_3	34.07	7.55	35.09	7.04	0.165 β
Discharge HCO_3	38.75	8.54	35.74	4.82	0.188 β
Follow-up HCO_3	30.65	5.23	31.81	6.26	0.403*
Hospitalization SaO_2	83.59	14.33	84.81	14.07	0.794 β
Discharge SaO_2	88.01	8.46	87.18	11.00	0.960 β
Follow-up SaO_2	88.09	9.75	83.36	16.28	0.338 β

Continuous variables were expressed as mean±standard deviation (SD). Independent samples t-test *, Mann-Whitney U Test β, p<0.05

Table 6. ROC analysis for discharge $PaCO_2$ levels and mortality periods

	n (%)	AUC	SE	p	95% CI
1-month mortality	17 (6.9)	0.630	0.066	0.073	(0.501-0.759)
3-month mortality	31 (12.7)	0.594	0.053	0.090	(0.491-0.698)
6-month mortality	46 (18.8)	0.585	0.045	0.074	(0.496-0.674)
8-month mortality	57 (23.3)	0.594	0.041	0.034	(0.512-0.675)
12-month mortality	68 (27.8)	0.561	0.040	0.140	(0.483-0.640)
General mortality	88 (35.9)	0.547	0.039	0.222	(0.471-0.623)

Test Result Variable(s): Discharge $PaCO_2$, AUC: Area, under the ROC Curve, SE: Standard Error, CI: Confidence interval

DISCUSSION

It is well-known that NIV use reduces dyspnea and dead space ventilation in patients presenting with COPD exacerbation, improves hypoventilation through increased minute ventilation, and, in turn, promotes gas exchange and regresses hypercapnia. NIV becomes the top-favored ventilator modality thanks to the mentioned positive impacts and since reducing the need for intubation and morbidity/mortality rates in patients with acute/chronic hypercapnia and acute/chronic respiratory failure (12).

The guideline by the 2020 Indian Society of Intensive Care (ISCCM) suggests robust evidence and strictly recommends NIV use in treating acute exacerbation of COPD in patients with acute or chronic acute respiratory acidosis (pH=7.25-7.35). However, it is not recommended to use NIV therapy routinely in normo-

or mildly hypercapnic patients with acute exacerbation of COPD without acidosis (pH>7.35) (13). Following the relevant guidelines, we did not administer NIV treatment to patients hospitalized in a GICU and those found to be hypercapnic without acidosis (n=79; 32.4%).

Arpağ et al. (14) evaluated the NIV response in acute hypercapnic respiratory failure and concluded that 41.7% of the patients whose hypercapnic acidosis rapidly improved with NIV treatment relapsed into respiratory acidosis shortly after switching to nasal oxygen. They also reported that acidosis status may vary depending on whether hypercapnia is acute or chronic and that patients need to be followed up in an ICU. Among our patients, those who were stable hypercapnic and were not given NIV were not included in the case group "who rapidly developed acidosis after switching to nasal oxygen," as determined by Arpağ et al. (14). In our center, NIV is often prescribed for home use to patients who rapidly develop acidosis.

In their study, Meservey et al. (15) examined readmission and mortality after discharge in patients with hypercapnic respiratory failure. The logistic regression analysis yielded that advanced age, active smoking, history of intubation at hospitalization, primary heart disease, congestive heart failure, peripheral vascular disease, history of malignancy, COPD, home oxygen use, low PaO_2 level, high serum HCO_3 level, and readmission in the first 30 days were found to be associated with mortality after discharge. They reported that the mortality risk increased by 1.39 for each unit increase in the Charlson comorbidity index (CI 1.09-1.76). The corrected mortality rates were high in those rehospitalized after discharge. In addition, mortality was found to be high in the first few months after discharge from the hospital.

We discovered that advanced age, congestive heart failure, coronary artery disease, and atrial fibrillation were significantly higher in the mortality group. Yet, the groups did not significantly differ by the presence of other comorbidities and clinical and laboratory findings. We also did not find a relationship between readmission to the hospital and mortality. On the contrary, we found that the readmission rate was higher in the survivor group probably since access to healthcare services in our country may be more convenient compared to other countries.

Baykal and Bulcun uttered that chronic hypoxemia in patients with COPD causes pulmonary vascular remodeling, leading to an increase in pulmonary artery pressure (16). Indeed, in our study, 88.5% (n=217) of the patients discharged with high partial carbon dioxide pressures were using home oxygen therapy. Thus, we may assert that the chronic hypoxemic and moderate hypercapnic clinical courses may have caused pulmonary hypertension, which can be explained by the significant divergence of mortality between the two groups due to heart-related diseases.

Borel et al. (17) found that cardiovascular comorbidities were the only independent factor associated with a higher risk of death in patients diagnosed with hypercapnic obesity hypoventilation syndrome and treated with long-term domiciliary NIV. In this study, we discovered no difference in $PaCO_2$ between the groups but a relationship between cardiac comorbidities and mortality. This finding may be related to the inability to meet the cardiac oxygen requirement due to hypoxemia. In their study, Şahan and Bulut (18) reported that hypoxia increases, pulmonary hypertension appears, and some changes occur in the right heart as the clinical severity of COPD progresses, which leads to atrial fibrillation.

Goedemans et al. (19) stated that the risk of acute myocardial infarction is increased in COPD patients due to similar pathophysiological mechanisms. They also reported that the risk of developing heart failure and cardiac arrhythmia is more common in COPD patients. In our study, we found that the rates of congestive heart failure, coronary artery disease, and atrial fibrillation were significantly higher in the mortality group.

Dretzke et al. (20) recruited thirty-one studies in their meta-analysis of the clinical outcomes of using domiciliary NIV in stable and newly discharged COPD patients. The findings showed no evidence of survival benefit of NIV use for stable patients, yet a possible trend to decrease hospitalization and improve quality of life. In our study, we found cardiac comorbidities to be factors affecting survival in stable and newly discharged hypercapnic patients who did not use domiciliary NIV and found the $PaCO_2$ cut-off value, showing a statistically significant difference in mortality at 8 months, to be 50.25 mmHg. Kohnlein et al. (21) proposed an algorithm for indications for long-term (domiciliary) NIV use, adapted from the German National Guidelines, in their systematic review. In this algorithm, long-term (domiciliary) NIV therapy is recommended:

- if the acute hypercapnic respiratory failure is developed in COPD exacerbation and NIV is utilized for treatment,
- if $PaCO_2$ level is >53 mmHg for 14 days, or diurnal $PaCO_2$ is >50 mmHg,
- if chronic respiratory failure symptoms are present, or nocturnal $PaCO_2$ is >50 mmHg, or diurnal $PaCO_2$ is between 45-50 mmHg, and nocturnal $PtcCO_2$ increases >10 mmHg.

Chu et al. (22) recruited 110 patients in their study, administered NIV therapy to those with COPD exacerbation and acute hypercapnic respiratory failure, and followed up survivors after discharge. The findings revealed the rate of readmission within a year to be 79.9%, the rate of life-threatening exacerbation to be 63.3%, and the overall mortality rate to be 49.1% . In our study, the rate of readmission in the first year was 64.5%, and the overall mortality rate was 35.9%.

Wilson et al. (23) reported that every 5 mmHg increase in $PaCO_2$ was associated with a significant increase in mortality from all causes in compensated hypercapnic patients. Suraj et al. (24) reported the effects of long-term use of domiciliary NIV use in their study. In their study consisting of patients hospitalized and discharged after more than three episodes of acute hypercapnic respiratory failure due to COPD in the last year, they showed that mortality, intensive care admissions, and hospitalizations decreased in the NIV group compared to the non-administered group. However, there were only 30 patients in the NIV group, and the follow-up period was only a year in this study.

In their meta-analysis, Xue He et al. (25) evaluated the efficacy of domiciliary NIV therapy in patients discharged after a COPD exacerbation. They reported that the frequency of exacerbations was significantly reduced in patients receiving domiciliary NIV. However, there were no significant differences in mortality, gas exchange (PaO_2, $PaCO_2$), and pH.

The relevant literature hosts conflicting data on the effect of long-term NIV use on mortality. However, there is a plethora of studies showing that hypercapnia increases the mortality rate, albeit moderately. In our study, we revealed that mortality increased especially among patients with heart-related disease accompanying mild hypercapnia, which is consistent with the literature.

Its retrospective design and the use of single-center data may be considered the major limitations of our study. In addition, the follow-up period can be counted among the limitations. We used exactly 24 months of patient data to avoid bias due to seasonal variability in COPD exacerbations and respiratory failure episodes.

CONCLUSION

We investigated the characteristics of the patients who were hospitalized with acute hypercapnic respiratory failure due to COPD exacerbation and discharged with moderate hypercapnia despite pH compensation (67.6%) or who were administered NIV in their treatment during the hospitalization. The findings uncovered the $PaCO_2$ cut-off level as 50.25 mmHg to predict 8-month mortality. While we could not reach significant differences between the groups by discharge $PaCO_2$ levels, the rates of heart-related diseases (e.g., congestive heart failure, coronary artery disease, and atrial fibrillation) were significantly higher in the mortality group. We assume that domiciliary NIV therapy needs to be considered among patients with mild hypercapnia ($PaCO_2$>50 mmHg) at discharge and with concomitant heart-related diseases. Further research may employ a larger sample size to engage in a more extensive investigation on the subject.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Health Sciences University Keçiören Training and Research Hospital, Clinical Research Ethics Committee (Date: 11.09.2021, Decision No: 2012-KAEK-15/2405).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version

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